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EXAMINER	
WITZ, J	
ART UNIT	**PAPER NUMBER**
1808	5

18M2/0529

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DATE MAILED: 05/29/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 12/18/95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), No days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-18 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-18 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

Part III DETAILED ACTION

Response to Amendment

1. Applicant's arguments filed December 18, 1995 have been fully considered but they are not deemed to be persuasive.

Specification

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification remains objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure and an adequate written description of the invention for the reasons of record.

Applicants argue that the object of the invention is to "reduce the amount of adipose tissue at selected locations in the body. If that is done, it matters not where the fat goes or whether the patient gains or loses overall weight. The invention has utility as described."

First it is noted that the Examiner questioned several aspects of the enablement of the claimed invention. First,

Applicants disclose this method as an alternative to liposuction. The object of the claimed invention is drawn to a cosmetic alteration of the body. Applicants' showing is drawn to the injection of the claimed proteinase(s) into fat pads of rats followed by autopsy and visual inspection and weight of the fat pads after up to 14 days.

With the procedure of liposuction, adipose tissue, comprised of adipocytes containing fat globules, is physically removed from the body, thereby reducing the absolute amount of fat present in the body at selected sites compared to those sites prior to the treatment. With the procedure of the claimed invention, while the connective tissue, i.e. the adipocytes, are broken apart from each other and broken open, the fat is still present in the body and the body must deal with it in some manner. Applicants make a statement at page 6 of the specification that "residue from adipose tissue in the treated location is at least partly metabolized." Applicants have in no way shown this to be true in a degree significant for the intent of the claimed invention. Unless the basal metabolism of the patient changes significantly, the fat present in the body will be maintained at its present level and will be deposited in adipocytes, either remaining at the site or at other sites, until metabolized. Applicants themselves indicate that rats treated as claimed for 14 days gained weight. See page 25, line 17 of the specification.

Clearly, it must matter "where the fat goes", if nothing is removed from the body. As fat deposited in adipose tissue has mass and therefore weight, clearly an increase in weight must matter "whether the patient gains or loses overall weight." Applicants' response of "so what" fails to address this consideration.

Finally, Applicants' arguments regarding the Guidicelli et al. reference are that "what happens metabolically is irrevelant [sic] to applicants' invention." An animal model should be reasonably predictive of a response in humans, which are the intended recipient of the claimed method steps. The Examiner has provided evidence that said animal model, the rat model, appears to be unable to predict efficacy in humans as it is clear from the reference that rat adipocytes react in a metabolically different manner from human adipocytes particularly when treated with collagenase and trypsin. Applicants' mere statement that this teaching is irrelevant is not persuasive.

Therefore, the showing of record remains insufficient to enable the claimed invention as it would require the practitioner to engage in an undue amount of experimentation to practice the claimed invention and the practitioner would still not have a reasonable expectation of success.

Claim Rejections - 35 USC § 112

3. Claims 1-18 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5. Claims 1-18 are rejected under 35 U.S.C. § 103 as being unpatentable over Lee et al. combined with Guidicelli et al. for the reasons of record.

Applicants argue that Lee teaches the disruption of liposuctioned fat after its removal from the body and concludes that Lee "ignores and teaches away from what applicants have discovered."

It is noted that the claims are drawn only to the reduction of adipose tissue at selected sites in the body comprising the introduction of collagenase and another proteinase into said tissue. Applicants themselves argue in the response to the rejection under 35 USC 112, 1st paragraph, that such reduction of adipose tissue, i.e. disruption of fat cells, is all that they claim. Applicants argue that any other considerations other than the disruption of fat cells is not germane.

Lee teaches that collagenase plus chymopapain digests, i.e. disrupts, connective tissue. Adipose tissue, a type of connective tissue, is particularly disclosed as being effectively disrupted so as to obtain endothelial cells present therein. Guidicelli et al. discloses that is conventional to use collagenase and trypsin for the purpose of digesting and isolating adipocytes.

It is noted that the Lee et al. reference discloses the effects of the claimed composition both in vitro and for in vivo therapeutic application for the digestion of connective tissue wherever desired. See col. 5, lines 14-21. Further, the claims call only for the reduction of adipose tissue, i.e., the disruption or digestion of adipose tissue, and per Applicants' statements in the response to the previous office action, such is all that is required. It would have been obvious and predictable to one of ordinary skill in the art to use conventional enzymes

known to digest said tissue, regardless of its site the expected digestion, i.e. dissociating the cells of the tissue at any location in the body or in tissue outside of the body. Optimization of dose is well within the skill of the practitioner as the enzyme kinetics of collagenase and other enzymes based upon amount of substrate are well known.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073.

JCW
May 28, 1996

MICHAEL G. WITYSHYN
SUPERVISORY PATENT EXAMINER
GROUP 1800
5-28